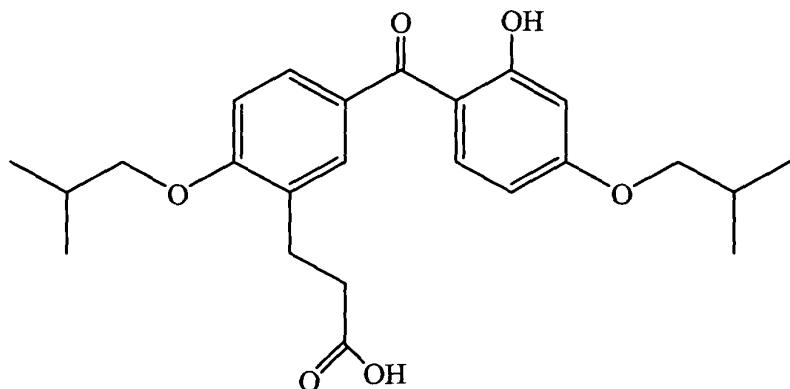


ELECTION OF SPECIES

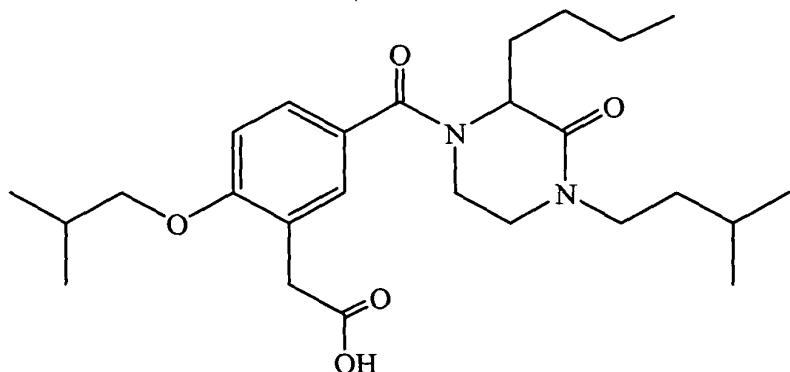
Applicants have also elected species of benzene derivatives of Claims 9, 12, 14, 16, 18, 20, 22, 24, 26, and 28 as indicated below. Applicants note that the Office required an election of a specie of benzene derivative of Claim 19. However, since Claim 19 depends from Claim 18, Applicants presume that the Examiner intended to require an election of a specie of benzene derivative of Claim 20, rather than Claim 19.

Claim 9: The compound of Example 38 having the formula shown below:

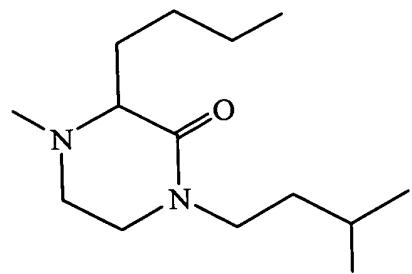


where R¹ is O-iBu, R³ is OH, R⁴ is O-iBu, X¹ is -C (O)-, and W is -CH₂CH₂COOH.

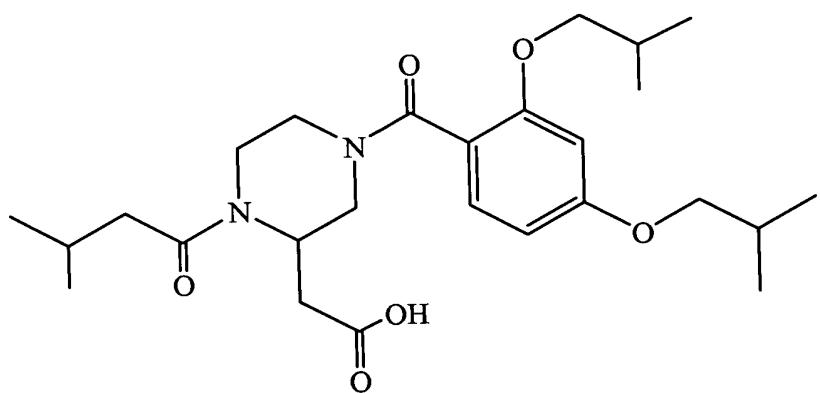
Claim 12: The compound in the first line of Table 2 having the formula:



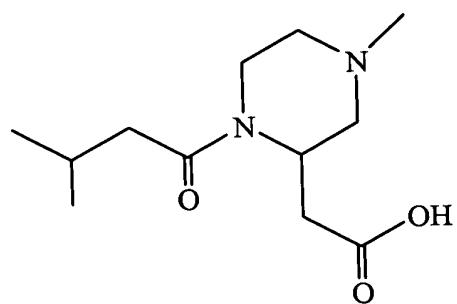
where R⁵ is O-iBu, R⁶ is H, X² is -C (O)-, m=1, and A is



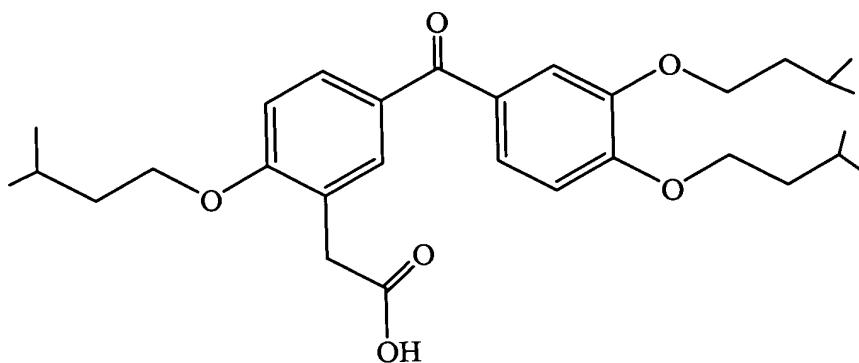
Claim 14: The compound in the 8th line of Table 4 having the formula:



where R¹⁵ is O-iBu, R¹⁶ is O-iBu, X³ is -C (O)-, and B is

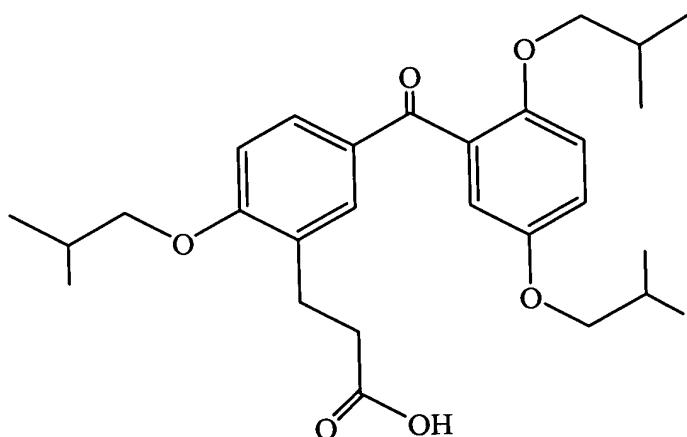


Claim 16: The compound of Example 46 having the formula:



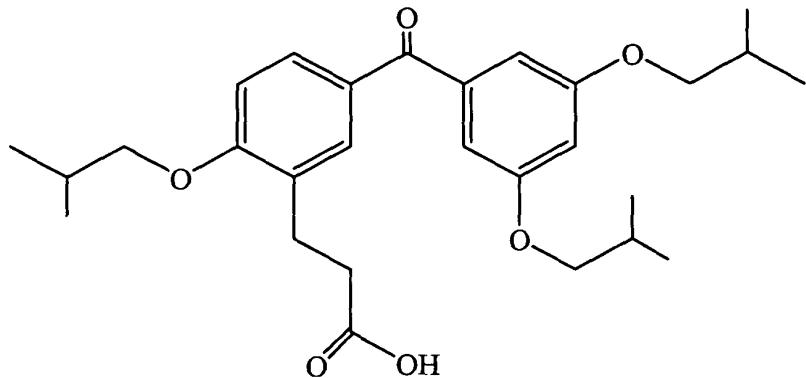
where R^{1a} is O-iAm , R^{3a} is O-iAm , R^{4a} is O-iAm , X^{1a} is $-\text{C}(\text{O})-$, W^a is CH_2COOH .

Claim 18: The compound of Example 43 having the formula:



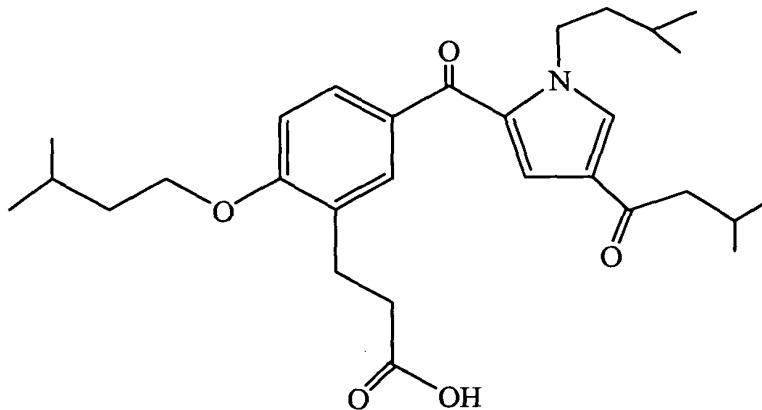
where R^{1b} is O-iBu , R^{2b} is H , R^{3b} is O-iBu , R^{4b} is O-iBu , X^{1b} is $-\text{C}(\text{O})-$, and Z^b is $-\text{CH}_2\text{CH}_2-$.

Claim 20: The compound of Example 41 having the formula:



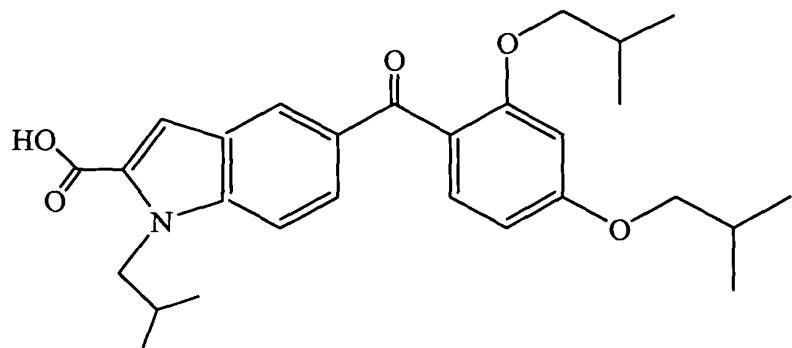
where R^{1c} is O-iBu, R^{2c} is H, R^{3c} is O-iBu, R^{4c} is O-iBu, X^{1c} is -C (O)-, and Z^c is -CH₂CH₂-.

Claim 22: The compound of Example 87 having the formula:



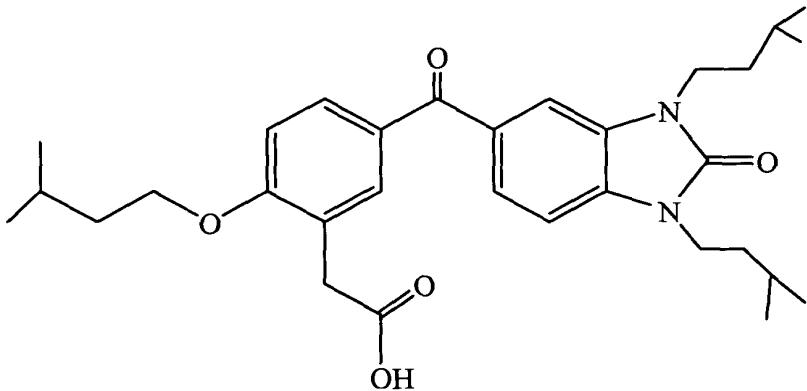
where R^{1d} is O-iAm, R^{2d} is H, R^{3d} is iAm, R^{4d} is -C (O) CH₂CH (CH₃)₂, X^{1d} is -C (O)-, and Z^d is -CH₂CH₂-.

Claim 24: The compound of Example 82 having the formula:



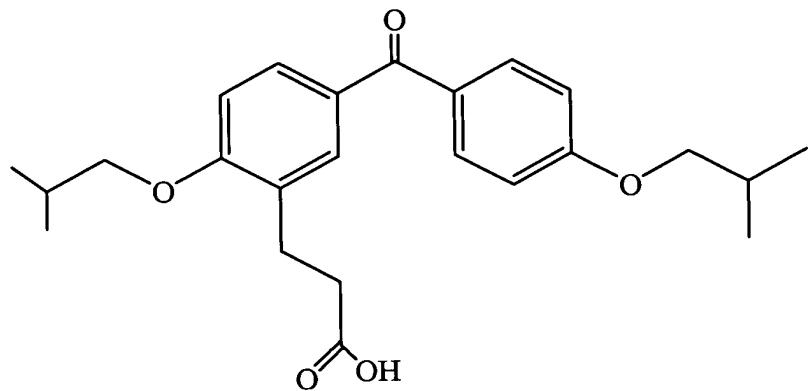
where R^{0e} is H, R^{1e} is iBu, R^{2e} is H, R^{3e} is O-iBu, R^{4e} is O-iBu, X^{1e} is -C (O)-, and Z^e is a chemical bond (i.e., -(CH₂)₀-).

Claim 26: The compound of Example 90 having the formula:



where R^{1f} is O-iAm, R^{2f} is H, R^{3f} is iAm, R^{4f} is iAm, X^{1f} is -C (O)-, and Z^f is -CH₂-.

Claim 28: The compound of Example 25(8) having the formula:

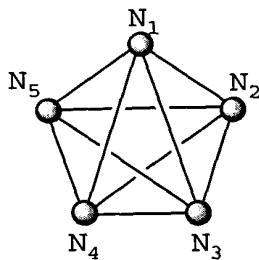


where R^{1g} is O-iBu, R^{2g} is H, R^{4g} is O-iBu, X^{1g} is -C (O)-, and Z^g is -CH₂CH₂-.

AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

Claim 1 (Original): A compound comprising the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅, said atoms constitute the pharmacophore represented by the following formula 1:



wherein N₁ represents an atom to which a donative hydrogen atom in a hydrogen-bond donating group is bonded or a hydrogen-bond accepting atom in a hydrogen-bond accepting group; N₃ represents a hydrogen-bond accepting atom in a hydrogen-bond accepting group; and N₂, N₄ and N₅ independently represent an arbitrary carbon atom constituting a hydrophobic group and the distance between N₁ and N₂ is not less than 5 angstroms and not more than 12 angstroms, the distance between N₁ and N₃ is not less than 9 angstroms and not more than 15 angstroms, the distance between N₁ and N₄ is not less than 3 angstroms and not more than 13 angstroms, the distance between N₁ and N₅ is not less than 8 angstroms and not more than 16 angstroms, the distance between N₂ and N₃ is not less than 3 angstroms and not more than 10 angstroms, the distance between N₂ and N₄ is not less than 6 angstroms and not more than 14 angstroms, the distance between N₂ and N₅ is not less than 9 angstroms and not more than 14 angstroms, the distance between N₃ and N₄ is not less than 4 angstroms and not more than 11 angstroms, the distance between N₃ and N₅ is not less than 3 angstroms and not more than 10 angstroms, and the distance between N₄ and N₅ is not less

than 4 angstroms and not more than 9 angstroms; and, in the optimized three-dimensional structure thereof, the distances between the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅ are the interatomic distances in the pharmacophore; and a salt thereof.

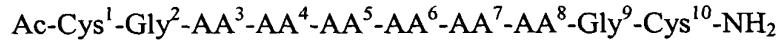
Claim 2 (Original): A compound or a salt thereof according to Claim 1, wherein, for each of the atoms constituting the pharmacophore, the distance between N₁ and N₂ is not less than 5.09 angstroms and not more than 11.67 angstroms, the distance between N₁ and N₃ is not less than 9.47 angstroms and not more than 14.30 angstroms, the distance between N₁ and N₄ is not less than 3.48 angstroms and not more than 12.60 angstroms, the distance between N₁ and N₅ is not less than 8.77 angstroms and not more than 15.67 angstroms, the distance between N₂ and N₃ is not less than 3.78 angstroms and not more than 9.78 angstroms, the distance between N₂ and N₄ is not less than 6.97 angstroms and not more than 13.26 angstroms, the distance between N₂ and N₅ is not less than 9.37 angstroms and not more than 13.32 angstroms, the distance between N₃ and N₄ is not less than 4.83 angstroms and not more than 10.51 angstroms, the distance between N₃ and N₅ is not less than 3.31 angstroms and not more than 9.97 angstroms, and the distance between N₄ and N₅ is not less than 4.32 angstroms and not more than 8.25 angstroms.

Claim 3 (Previously Presented): A compound or a salt thereof according to Claim 1, wherein N₁ constituting the pharmacophore is a nitrogen atom of unsubstituted or substituted amino, ammonium, amido, thioamido, ureido, isoureido, amidino, guanidino, thioureido, hydrazino or hydrazone group to which one or more hydrogen atoms are bonded, a carbon atom of ethenyl group to which a hydrogen atom is bonded, an oxygen atom of carbonyl group, a sulfur atom of thiocarbonyl group, a nitrogen atom of unsubstituted or substituted

imino group, an oxygen atom of sulfonyl group, an oxygen atom of sulfonyloxy group, an oxygen atom of sulfo group, an oxygen atom of sulfinyl group, an oxygen atom of carboxyl group, an oxygen atom of ether, a sulfur atom of thioether, a sulfur atom of mercapto group, an oxygen atom of hydroxyl group, an oxygen atom of ester or a nitrogen atom of unsubstituted or substituted nitrogen-containing heterocyclic group; N₃ is an oxygen atom of carbonyl group, a sulfur atom of thiocarbonyl group, a nitrogen atom of unsubstituted or substituted imino group, an oxygen atom of sulfo group, an oxygen atom of sulfonyl group, an oxygen atom of sulfo group, an oxygen atom of sulfonyloxy group, an oxygen atom of carboxyl group, an oxygen atom of ether, a sulfur atom of thioether, an oxygen atom of hydroxyl group, an oxygen atom of ester, a nitrogen atom of unsubstituted or substituted nitrogen-containing heterocyclic group to which no hydrogen atom is combined, a nitrogen atom of sulfonamido group or a nitrogen atom of acylsulfonamido group; and each of N₂, N₄ and N₅ is an arbitrary carbon atom constituting a carbon atom of alkyl group, a carbon atom of alkenyl group, a carbon atom of aryl group and a carbon atom of alkoxy group.

Claim 4 (Previously Presented): A compound or a salt thereof according to Claim 1, wherein a compound having an atom corresponding to N₃ and atoms corresponding to two or more atoms selected from N₁, N₂, N₄ and N₅ among the atoms N₁, N₂, N₃, N₄ and N₅ constituting a pharmacophore, and, in the optimized three-dimensional structure thereof, the interatomic distances between the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅ are the atomic distances of a pharmacophore has an activity of antagonistically inhibiting the binding between AP-1 (activator protein-1) and a recognition sequence thereof.

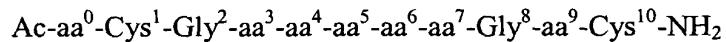
Claim 5 (Original): A peptide of 10 residues represented by the following amino acid sequence:



wherein Ac represents an acetyl group, AA³ represents a polar amino acid residue, each of AA⁴, AA⁶ and AA⁷ represents a hydrophobic amino acid residue, AA⁵ represents an amino acid residue having carboxyl or hydroxyl group in the side chain thereof, and AA⁸ represents an arbitrary amino acid residue; said peptide having a disulfide linkage between the first and tenth cysteine residues; or a salt thereof.

Claim 6 (Original): A peptide or a salt thereof according to Claim 5, wherein AA³ is an L-asparagine residue or an L-glutamine residue; AA⁴, AA⁶ and AA⁷ are an L-leucine residue, an L-isoleucine residue, an L-alanine residue or an L-valine residue; and AA⁵ is an L-aspartic acid residue, an L-glutamic acid residue, an L-serine residue or an L-threonine residue.

Claim 7 (Original): A peptide of 10 or 11 residues represented by the following amino acid sequence:



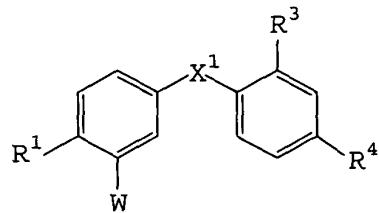
wherein Ac represents an acetyl group, aa⁰ represents an arbitrary amino acid residue or a bonding unit, aa³ represents a polar amino acid residue, each of aa⁴, aa⁵ and aa⁷ represents a hydrophobic amino acid residue, aa⁶ represents an arbitrary amino acid residue, and aa⁹ represents an amino acid residue having carboxyl or hydroxyl group in the side chain thereof; provided that, when aa⁰ is a bonding unit, said peptide has a disulfide linkage between the first and tenth cysteine residues and, when aa⁰ is an arbitrary amino acid residue,

Application No. 09/830,559
Reply to Office Action of July 16, 2003

said peptide has a disulfide linkage between the second and eleventh cysteine residues; or a salt thereof.

Claim 8 (Original): A peptide or a salt thereof according to Claim 7, wherein aa³ is an L-asparagine acid residue or an L-glutamine acid residue; aa⁴, aa⁵ and aa⁷ are an L-leucine residue, an L-isoleucine residue, an L-alanine residue or an L-valine residue; and aa⁹ is an L-aspartic acid residue, an L-glutamic acid residue, an L-serine residue or an L-threonine residue.

Claim 9 (Original): A benzene derivative represented by the following general formula:

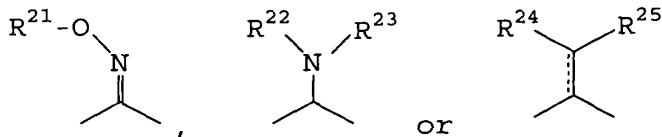


wherein R¹ represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R³ represents a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group, a carbamoyl group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, alkylthio,

Reply to Office Action of July 16, 2003

alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R⁴ represents a hydrogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group;

X¹ represents -C(O)-, -CH(OH)-, -CH₂- or a group of the following formula:



wherein R²¹ represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl or heterocycle-lower alkyl group; R²² and R²³ may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, arylsulfonyl or heterocyclic group; and R²⁴ and R²⁵ may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; the double line of which one line is a broken line denotes a single bond or a double bond; and

W represents -Z-COR²⁶, -Z-COOR², -O-CH₂COOR² or -O-CH₂CH₂COOR² [wherein Z represents -(CH₂)_n- in which n represents 0, 1, 2 or 3, -CH₂CH(CH₃)-, -CH=CH- or -

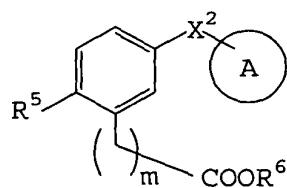
Application No. 09/830,559
Reply to Office Action of July 16, 2003

CH₂CH=CH-; R² represents a hydrogen atom or a protecting group for carboxyl group; and R²⁶ represents -NHR²⁷ or -NHSO₂R²⁸ in which R²⁷ and R²⁸ independently represent an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group]; or a salt thereof.

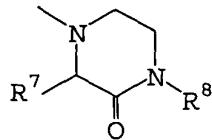
Claim 10 (Original): A benzene derivative or a salt thereof according to Claim 9, wherein W is -Z'-COOR^{2'}, -Z'-CONH-SO₂R^{28'}, -CONH-CH₂COOR^{2'} or -CONH-CH₂CH₂COOR^{2'} [wherein Z' represents -(CH₂)_{n'}- in which n' is 0, 1 or 2, or -CH=CH-; R^{28'} represents an unsubstituted or substituted alkyl group; and R^{2'} represents a hydrogen atom or a protecting group for carboxyl group]; and X¹ is -C(O)-, -CH(OH)- or -CH₂-.

Claim 11 (Original): A benzene derivative or a salt thereof according to Claim 10, wherein R¹ is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; R³ is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; and R⁴ is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group.

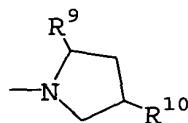
Claim 12 (Original): A benzene derivative represented by the following general formula:



wherein R⁵ represents a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonlamino, arylsulfonlamino or heterocyclic group; R⁶ represents a hydrogen atom or a protecting group for carboxyl group; X² represents -C(O)-; m represents 0, 1 or 2; and ring A represents a group represented by the following formula:

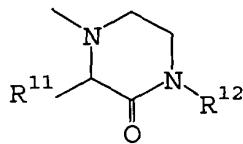


wherein R⁷ represents a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonlamino, arylsulfonlamino or heterocyclic group; and R⁸ represents a hydrogen atom, an unprotected or protected amino group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonlamino, arylsulfonlamino or heterocyclic group; or a group of the following formula:

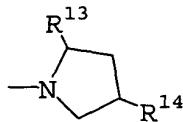


wherein R⁹ and R¹⁰ may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino, alkanoyloxy or heterocyclic group;
or a salt thereof.

Claim 13 (Original): A benzene derivative or a salt thereof according to Claim 12, wherein R⁵ is an alkoxy group or an acylamino group; X² is -C(O)-; and ring A is a group of the following formula:

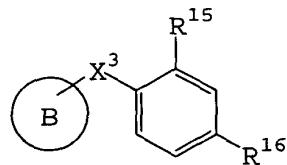


wherein R¹¹ is an alkyl or alkoxycarbonyl group; and R¹² is an alkyl group; or a group of the following formula:

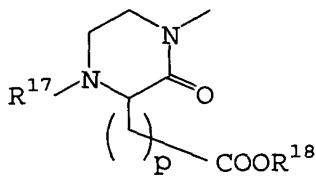


wherein R¹³ is an alkyl or alkoxy carbonyl group; and R¹⁴ is an alkoxy or alkanoyloxy group.

Claim 14 (Original): A benzene derivative represented by the following general formula:

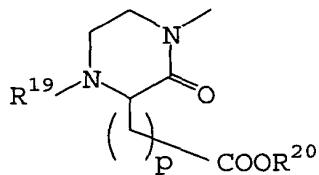


wherein R¹⁵ and R¹⁶ may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxy carbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X³ represents -C(O)-; and ring B represents a group of the following formula:



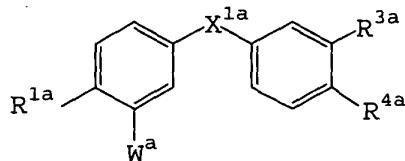
wherein R¹⁷ represents a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy carbonyl, aryloxycarbonyl, carbamoyl, alkylsulfonyl or heterocyclic group; R¹⁸ represents a hydrogen atom or a protecting group for carboxyl group; and p represents 0, 1 or 2;
or a salt thereof.

Claim 15 (Original): A benzene derivative or a salt thereof according to Claim 14, wherein R¹⁵ and R¹⁶ may be the same or different represent an alkoxy group; and ring B represents a group of the following formula:

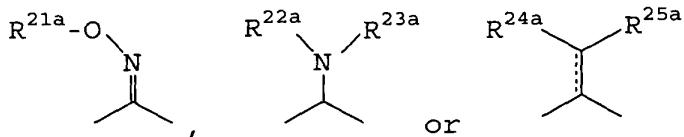


wherein R¹⁹ is an acyl group; R²⁰ is a protecting group for carboxyl group; and p is 0, 1 or 2.

Claim 16 (Previously Presented): A benzene derivative represented by the following formula:



wherein R^{1a} represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R^{3a} and R^{4a} may be the same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X^{1a} represents -C(O)-, -CH(OH)-, -CH₂- or a group of the following formula:

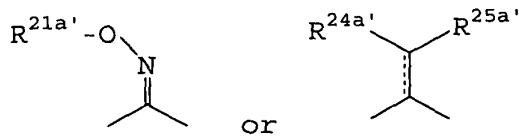


wherein R^{21a} represents an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl or heterocycle-lower alkyl group; R^{22a} and R^{23a} may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl,

Application No. 09/830,559
Reply to Office Action of July 16, 2003

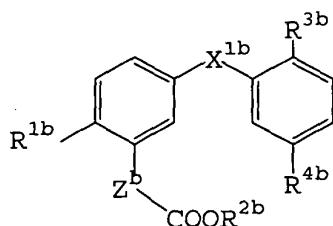
aralkyl, acyl, carbamoyl, alkylsulfinyl, alkylsulfonyl, arylsulfonyl or heterocyclic group; R^{24a} and R^{25a} may be the same or different represent a hydrogen atom, a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxy carbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; and the double line of which one line is a broken line represents a single bond or a double bond; and W^a represents -Z^a-COR^{26a}, -Z^a-COOR^{2a}, -O-CH₂COOR^{2a} or -O-CH₂CH₂COOR^{2a} [wherein Z^a represents -(CH₂)_n^a- (n^a is 1, 2 or 3), -CH₂CH(CH₃)-, -CH=CH- or -CH₂CH=CH-; R^{26a} represents -NHR^{27a} or -NHSO₂R^{28a} (R^{27a} and R^{28a} independently represent an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group)]; or a salt thereof.

Claim 17 (Original): A benzene derivative or a salt thereof according to Claim 16, wherein R^{1a} is an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; R^{3a} and R^{4a} may be the same or different and represent an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; X^{1a} is -C(O)-, -CH(OH)-, -CH₂- or a group of the following formula:



wherein $R^{21a'}$ represents an unsubstituted or substituted alkyl, aralkyl or heterocycle-lower alkyl group; $R^{24a'}$ and $R^{25a'}$ may be the same or different represent a hydrogen atom, an unprotected or protected carboxyl group or an unsubstituted or substituted alkyl, alkoxycarbonyl, aryloxycarbonyl or carbamoyl group; and W^a represents $-Z^{a'}-COR^{26a'}$, $-Z^{a'}-$ $COOR^{2a'}$, $-O-CH_2COOR^{2a'}$, $-O-CH_2CH_2COOR^{2a'}$, $-CONH-CH_2COOR^{2a'}$, or $-CONH-$ $CH_2CH_2COOR^{2a'}$ [wherein $Z^{a'}$ represents $-(CH_2)_n^{a'-}$ in which $n^{a'}$ is 0, 1, 2 or 3, $-CH_2CH(CH_3)-$, $-CH=CH-$ or $-CH_2CH=CH-$; $R^{2a'}$ represents a hydrogen atom or a protecting group for carboxyl group; and $R^{26a'}$ represents $-NHSO_2R^{28a'}$ in which $R^{28a'}$ is an unsubstituted or substituted alkyl group].

Claim 18 (Original): A benzene derivative represented by the following general formula:



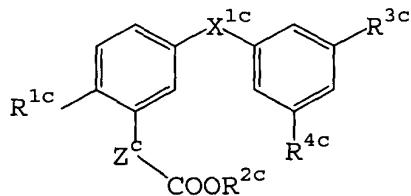
wherein R^{1b} represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R^{2b} represents a hydrogen atom or a protecting group for carboxyl group; R^{3b} and R^{4b} may be the same or different represent a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group,

Application No. 09/830,559
Reply to Office Action of July 16, 2003

a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X^{1b} represents $-C(O)-$, $-CH(OH)-$ or $-CH_2-$; and Z^b represents $-(CH_2)_n^b$ (n^b represents 0, 1 or 2) or $-CH=CH-$;
or a salt thereof.

Claim 19 (Original): A benzene derivative or a salt thereof according to Claim 18, wherein R^{1b} is an unsubstituted or substituted alkoxy group; R^{3b} and R^{4b} may be the same or different represent an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; X^{1b} is $-C(O)-$; and Z^b is $-(CH_2)_2-$.

Claim 20 (Original): A benzene derivative represented by the following general formula:



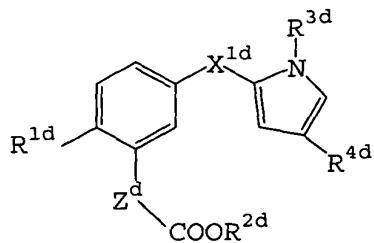
wherein R^{1c} represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R^{2c} represents a hydrogen atom or a protecting group for carboxyl group; R^{3c} and R^{4c} may be the

Application No. 09/830,559
Reply to Office Action of July 16, 2003

same or different represent a halogen atom, a cyano group, a nitro group, an unprotected or protected carboxyl group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl, alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; X^{1c} represents $-C(O)-$, $-CH(OH)-$ or $-CH_2-$; and Z^c represents $-(CH_2)_n^c$ - (n^c represents 0, 1 or 2) or $-CH=CH-$;
or a salt thereof.

Claim 21 (Original): A benzene derivative or a salt thereof according to Claim 20, wherein R^{1c} is an unsubstituted or substituted alkoxy group; R^{2c} is a hydrogen atom or a protecting group for carboxyl group; R^{3c} and R^{4c} may be the same or different represent an unsubstituted or substituted alkoxy group; X^{1c} represents $-C(O)-$; and Z^c represents $-(CH_2)_2-$.

Claim 22 (Original): A benzene derivative represented by the following general formula:



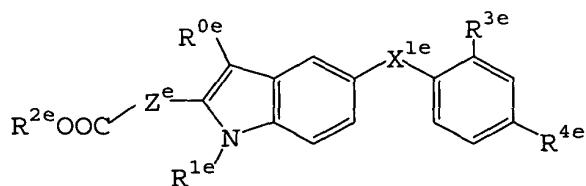
wherein R^{1d} represents a halogen atom, a cyano group, a nitro group, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, acyl,

Application No. 09/830,559
Reply to Office Action of July 16, 2003

alkoxycarbonyl, aryloxycarbonyl, carbamoyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R^{2d} represents a hydrogen atom or a protecting group for carboxyl group; R^{3d} represents a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group; R^{4d} represents a halogen atom, a nitro group, an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy carbonyl, aryloxycarbonyl, alkylsulfonyl, alkylsulfonylamino or arylsulfonylamino group; X^{1d} represents -C(O)-, -CH(OH)- or -CH₂-; and Z^d represents -(CH₂)_n^d - (n^d represents 0, 1 or 2) or -CH=CH-; or a salt thereof.

Claim 23 (Original): A benzene derivative or a salt thereof according to Claim 22, wherein R^{1d} is an unsubstituted or substituted alkoxy group; R^{3d} is an unsubstituted or substituted alkyl group; R^{4d} is an unsubstituted or substituted acyl group; X^{1d} is -C(O)-; and Z^d is -(CH₂)₂-.

Claim 24 (Previously Presented): A benzene derivative represented by the following general formula:



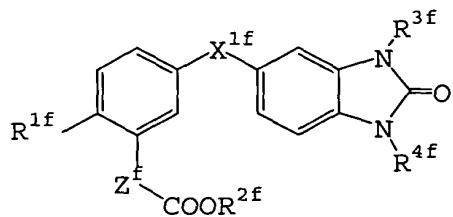
wherein R^{0e} represents a hydrogen atom, a halogen atom, a nitro group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxy carbonyl, aryloxycarbonyl, alkylsulfonylamino or arylsulfonylamino group; R^{1e} represents an

Application No. 09/830,559
Reply to Office Action of July 16, 2003

unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, acyl, alkoxycarbonyl, aryloxycarbonyl or alkylsulfonyl group; R^{2e} represents a hydrogen atom or a protecting group for carboxyl group; R^{3e} and R^{4e} may be the same or different represent a hydrogen atom, a halogen atom, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, alkylthio, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group, provided that both R^{3e} and R^{4e} cannot simultaneously be a hydrogen atom; X^{1e} represents -C(O)-, -CH(OH)- or -CH₂-; and Z^e represents -(CH₂)_n^e- (n^e represents 0, 1 or 2) or -CH=CH-; or a salt thereof.

Claim 25 (Original): A benzene derivative or a salt thereof according to Claim 24, wherein R^{0e} is a hydrogen atom or a halogen atom; R^{1e} is an unsubstituted or substituted alkyl group; R^{3e} and R^{4e} independently represent an unsubstituted or substituted alkoxy group; X^{1e} is -C(O)-; and Z^e is a bonding unit.

Claim 26 (Original): A benzene derivative represented by the following general formula:



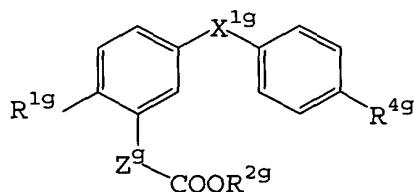
wherein R^{1f} represents a halogen atom, an unprotected or protected hydroxyl group, an unprotected or protected amino group, a mercapto group or an unsubstituted or substituted

- Application No. 09/830,559
Reply to Office Action of July 16, 2003

alkyl, alkenyl, cycloalkyl, aryl, aralkyl, alkoxy, aryloxy, alkylthio, alkylamino, acylamino, alkylsulfonylamino, arylsulfonylamino or heterocyclic group; R^{2f} represents a hydrogen atom or a protecting group for carboxyl group; R^{3f} and R^{4f} may be the same or different represent a hydrogen atom or an unsubstituted or substituted alkyl, alkenyl, cycloalkyl, aryl or aralkyl group; X^{1f} represents -C(O)-, -CH(OH)- or -CH₂-; and Z^f represents -(CH₂)_{n^f}- (n^f represents 1 or 2) or -CH=CH-; or a salt thereof.

Claim 27 (Original): A benzene derivative or a salt thereof according to Claim 26, wherein R^{1f} is an unsubstituted or substituted alkoxy group; R^{3f} and R^{4f} independently represent an unsubstituted or substituted alkyl group; X^{1f} is -C(O)-; and Z^f is -CH₂-.

Claim 28 (Original): A benzene derivative represented by the following general formula:

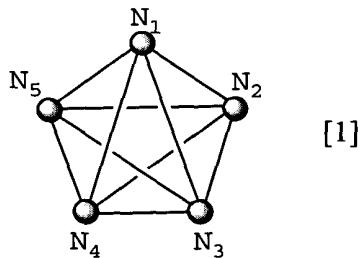


wherein R^{1g} and R^{4g} may be the same or different represent an unprotected or protected hydroxyl group or an unsubstituted or substituted alkoxy group; X^{1g} is -C(O)-, -CH(OH)- or -CH₂-; Z^g is -(CH₂)_{n^g}- (n^g represents 1 or 2); and R^{2g} is a hydrogen atom or a protecting group for carboxyl group;

or a salt thereof.

Claim 29 (Previously Presented): A compound or a salt thereof according to Claim 9, wherein said compound is a compound that has an activity of antagonistically inhibiting the combination between AP-1 and a recognition sequence thereof.

Claim 30 (Previously Presented): A compound comprising the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅, said atoms constitute the pharmacophore represented by the following formula 1:



wherein N₁ represents an atom to which a donative hydrogen atom in a hydrogen-bond donating group is bonded or a hydrogen-bond accepting atom in a hydrogen-bond accepting group; N₃ represents a hydrogen-bond accepting atom in a hydrogen-bond accepting group; and N₂, N₄ and N₅ independently represent an arbitrary carbon atom constituting a hydrophobic group and the distance between N₁ and N₂ is not less than 5 angstroms and not more than 12 angstroms, the distance between N₁ and N₃ is not less than 9 angstroms and not more than 15 angstroms, the distance between N₁ and N₄ is not less than 3 angstroms and not more than 13 angstroms, the distance between N₁ and N₅ is not less than 8 angstroms and not more than 16 angstroms, the distance between N₂ and N₃ is not less than 3 angstroms and not more than 10 angstroms, the distance between N₂ and N₄ is not less than 6 angstroms and not more than 14 angstroms, the distance between N₂ and N₅ is not less than 9 angstroms and not more than 14 angstroms, the distance between N₃ and N₄ is not less than 4 angstroms and not more than 11 angstroms, the distance between N₃ and N₅ is not less than 3 angstroms and not

- Application No. 09/830,559
Reply to Office Action of July 16, 2003

more than 10 angstroms, the distance between N₄ and N₅ is not less than 4 angstroms and not more than 9 angstroms; and, in the optimized three-dimensional structure thereof, the distances between the atom corresponding to N₃ and the two or more atoms selected from N₁, N₂, N₄ and N₅ are the interatomic distances in the pharmacophore; and a salt thereof, wherein the compound conforming to a pharmacophore is a peptide or a benzene derivative according to Claim 9.

Claim 31 (Previously Presented): A method for inhibiting AP-1 which comprises administering a compound or a salt thereof according to Claim 1.

Claim 32 (Previously Presented): An agent for preventing and treating a disease into which an excessive expression of AP-1 participates, which comprises a compound or a salt thereof according to Claim 1.

Claim 33 (Previously Presented): An agent for preventing and treating an autoimmune disease, which comprises a compound or a salt thereof according to Claim 1.

Claim 34 (Previously Presented): An AP-1 inhibitor comprising a compound or a salt thereof according to Claim 1.

Claim 35 (Previously Presented): A compound or a salt thereof according to Claim 9, wherein said compound is a compound that has an activity of antagonistically inhibiting the combination between AP-1 and a recognition sequence thereof.

Claim 36 (Cancelled).

Application No. 09/830,559
Reply to Office Action of July 16, 2003

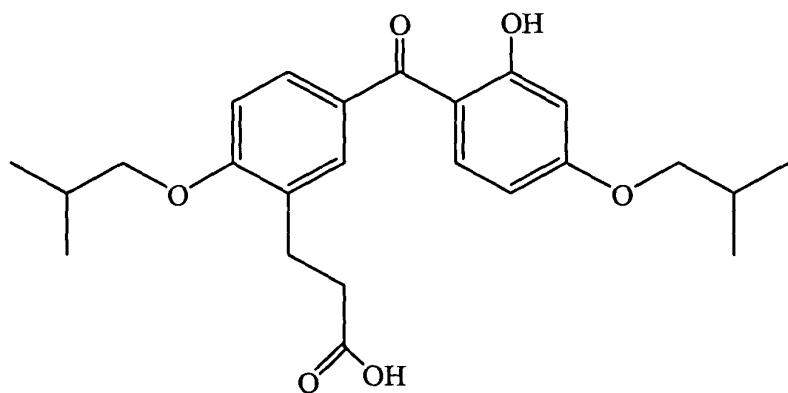
Claim 37 (Previously Presented): A method for inhibiting AP-1 which comprises administering a compound or a salt thereof according to Claim 9.

Claim 38 (Previously Presented): An agent for preventing and treating a disease into which an excessive expression of AP-1 participates, which comprises a compound or a salt thereof according to Claim 9.

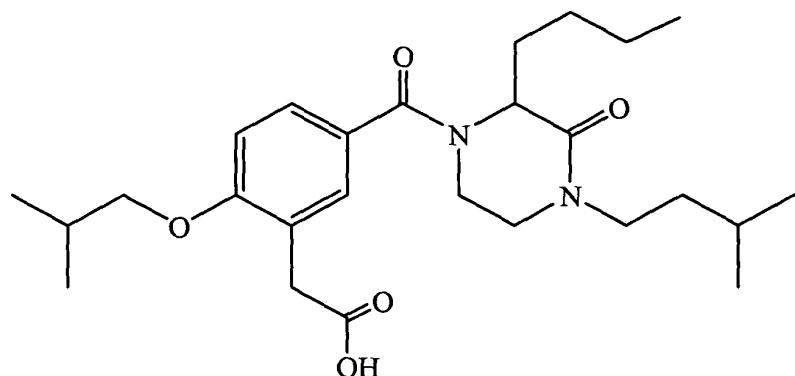
Claim 39 (Previously Presented): An agent for preventing and treating an autoimmune disease, which comprises a compound or a salt thereof according to Claim 9.

Claim 40 (Previously Presented): An AP-1 inhibitor comprising a compound or a salt thereof according to Claim 9.

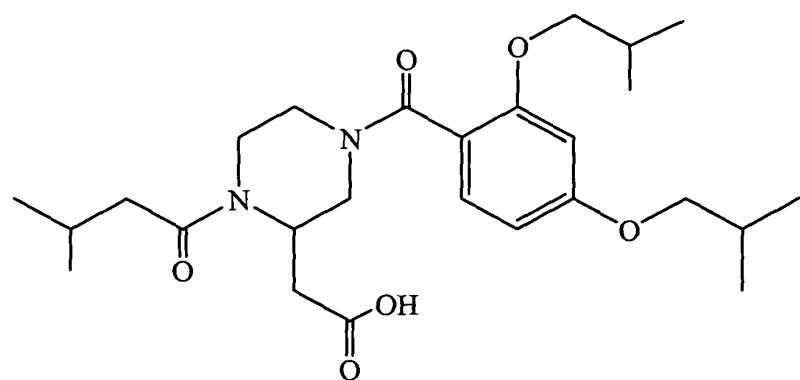
Claim 41 (New): A benzene derivative according to Claim 9, having the following formula:



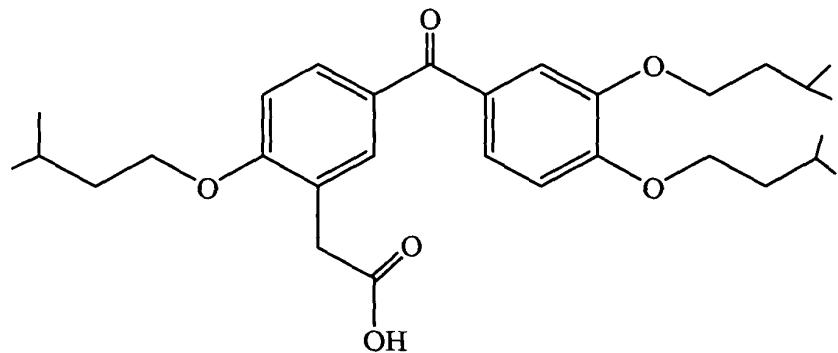
Claim 42 (New): A benzene derivative according to Claim 12, having the following formula:



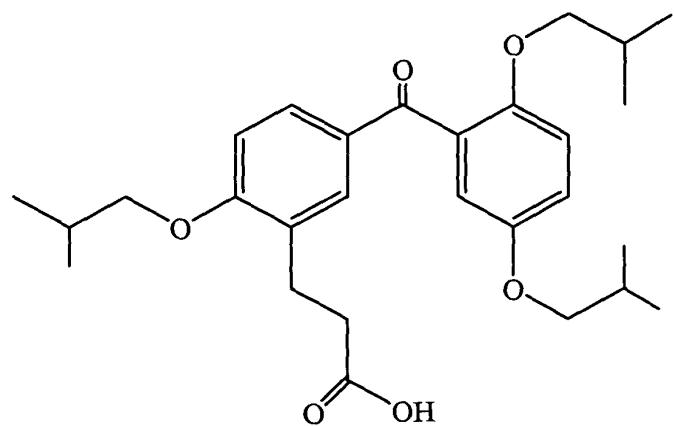
Claim 43 (New): The benzene derivative according to Claim 14, having the following formula:



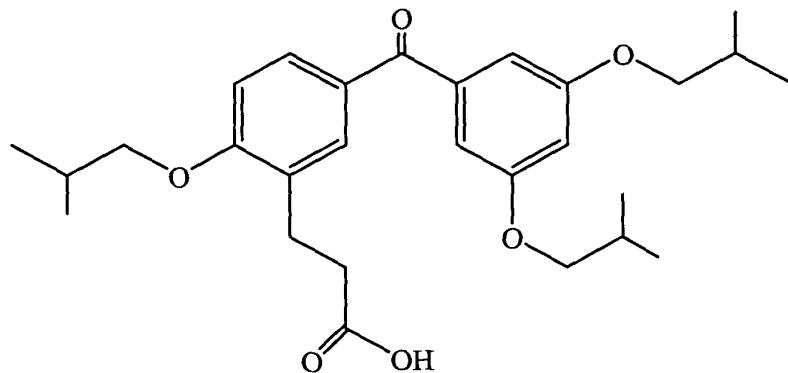
Claim 44 (New): A benzene derivative according to Claim 16, having the formula:



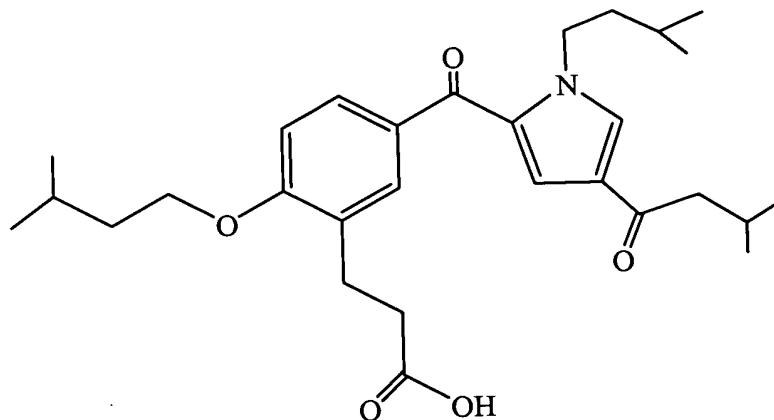
Claim 45 (New): A benzene derivative according to Claim 18, having the formula:



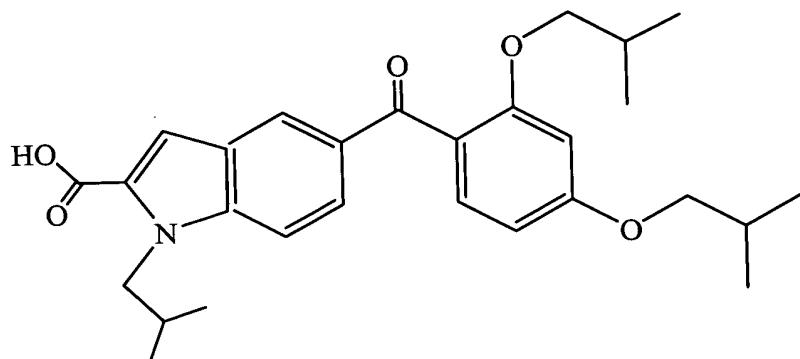
Claim 46 (New): The benzene derivative according to Claim 20, having the formula:



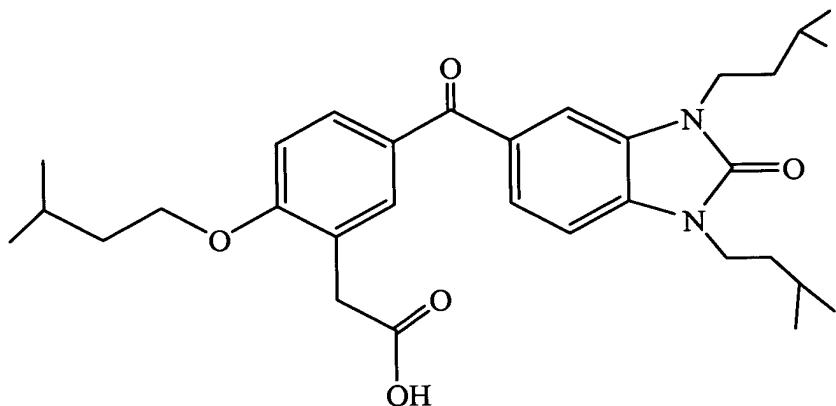
Claim 47 (New): The benzene derivative according to Claim 22, having the formula:



Claim 48 (New): The benzene derivative according to Claim 24, having the formula:



Claim 49 (New): The benzene derivative according to Claim 26, having the formula:



Claim 50 (New): The benzene derivative according to Claim 28, having the formula:

